

Appl. No. : 10/665,975
Filed : September 18, 2003

AMENDMENTS TO THE CLAIMS

1. **(Withdrawn)** A method for enhancing apoptosis of neoplastic cells comprising inhibiting interaction of hepatitis B X-interacting protein (HBXIP) with Survivin.
2. **(Withdrawn)** The method of Claim 1, further comprising using siRNA or antisense to downregulate expression of HBXIP.
3. **(Withdrawn)** The method of Claim 1, further comprising using HBXIP- or Survivin-specific antibodies to inhibit the interaction of HBXIP with Survivin.
4. **(Withdrawn)** The method of Claim 1, further comprising using specific inhibitors, molecular decoys, or the like to downregulate HBXIP.
5. **(Withdrawn)** A compound that inhibits HBXIP in the presence of Survivin.
6. **(Withdrawn)** A pharmaceutical composition comprising a compound that inhibits HBXIP in the presence of Survivin.
7. **(Withdrawn)** A method of treating neoplastic disease comprising administration of an inhibitor of HBXIP in the presence of Survivin.
8. **(Withdrawn)** A method for treating human liver disease associated with HBV, comprising administration of an inhibitor of HBXIP in the presence of Survivin.
9. **(Currently amended)** A compound that inhibits interaction of Survivin with hepatitis B X-interacting protein in the presence of (HBXIP), wherein said compound is selected from antisense nucleic acids complementary to at least a portion of the coding strand of the Survivin of SEQ ID NO: 1.
10. **(Currently amended)** A pharmaceutical composition comprising the compound of Claim 9 a compound that inhibits Survivin in the presence of HBXIP.
11. **(Withdrawn)** A method for identifying an effective agent that alters the association of Survivin and HBXIP comprising:
 - contacting Survivin and HBXIP under conditions that allow Survivin and HBXIP to associate in the presence or absence of a compound; and
 - detecting an altered association between Survivin and HBXIP, thereby determining whether said compound is an effective agent for altering association of Survivin with HBXIP.

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12. **(Withdrawn)** The method of Claim 11, wherein Survivin and HBXIP associate in the presence of a compound and pro-Caspase-9.

13. **(Withdrawn)** The method of Claim 11, wherein the altered association between Survivin and HBXIP is detected by measuring the activation of pro-Caspase-9.

14. **(Withdrawn)** A method for identifying an agent that effectively inhibits the activity of Survivin, comprising:

contacting Survivin with a cell extract containing HBXIP and pro-Caspase-9 in the presence of a compound;

inducing activation of pro-Caspase-9 using cytochrome C; and

measuring the activation of pro-Caspase-9, thereby determining whether said compound is an agent that effectively inhibits the activity of Survivin.

15. **(Withdrawn)** A method for identifying an agent that effectively inhibits the activity of HBXIP, comprising:

contacting HBXIP with a cell extract containing Survivin and pro-Caspase-9 in the presence of a compound;

inducing activation of pro-Caspase-9 using cytochrome C; and

measuring the activation of pro-Caspase-9, thereby determining whether said compound is an agent that effectively inhibits the activity of HBXIP.

16. **(Withdrawn)** A method for identifying an agent that effectively inhibits the activity of HBX, comprising:

contacting HBX with a cell extract containing Survivin and pro-Caspase-9 in the presence of a compound;

inducing activation of pro-Caspase-9; and

measuring the activation of pro-Caspase-9, thereby determining whether said compound is an agent that effectively inhibits the activity of HBX.

17. **(Withdrawn)** A method for identifying an agent that effectively inhibits the activity of Survivin, comprising:

contacting Survivin with purified pro-Caspase-9 and Apaf1 in the presence of HBXIP and a compound;

inducing activation of pro-Caspase-9; and

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measuring the activation of pro-Caspase-9, thereby determining whether said compound is an agent that effectively inhibits the activity of Survivin.

18. **(Withdrawn)** A method for identifying an agent that effectively inhibits the activity of HBXIP, comprising:

contacting HBXIP with purified pro-Caspase-9 and Apaf1 in the presence of Survivin and a compound;

inducing activation of pro-Caspase-9; and

measuring the activation of pro-Caspase-9, thereby determining whether said compound is an agent that effectively inhibits the activity of HBXIP.

19. **(Withdrawn)** A method for identifying an effective agent that alters the association of Survivin and HBXIP comprising:

contacting Survivin and HBXIP under conditions that allow Survivin and HBXIP to associate in the presence a compound, pro-Caspase-3, pro-Caspase-9, Apaf1 and cytochrome C; and

detecting an altered association between Survivin and HBXIP, thereby determining whether said compound is an effective agent for altering association of Survivin with HBXIP.

20. **(Withdrawn)** The method of Claim 19, wherein the altered association between Survivin and HBXIP is detected by measuring the activation of pro-Caspase-3.

21. **(Withdrawn)** The method of Claim 20, wherein the activation of pro-Caspase-3 is measured by monitoring the cleavage of a caspase 3 substrate selected from the group consisting of DEVD-AFC, DEVD-pNA and DEVD-AMC.

22. **(Withdrawn)** A method for identifying an effective agent that alters the association of Survivin and HBXIP comprising:

contacting Survivin and HBXIP under conditions that allow Survivin and HBXIP to associate in the presence a cell extract and a compound; and

detecting an altered association between Survivin and HBXIP, thereby determining whether said compound is an effective agent for altering association of Survivin with HBXIP.

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23. **(Withdrawn)** The method of Claim 22, wherein said cell extract comprises pro-Caspase-9 and pro-Caspase-3.

24. **(Withdrawn)** The method of Claim 22, wherein the altered association between Survivin and HBXIP is detected by measuring the activation of pro-Caspase-3.

25. **(Withdrawn)** The method of Claim 24, wherein the activation of pro-Caspase-3 is measured by monitoring the cleavage of a caspase 3 substrate selected from the group consisting of DEVD-AFC, DEVD-pNA and DEVD-AMC.

26. **(Withdrawn)** A method of identifying an agent that potentially alters the association of Survivin and HBXIP comprising:

identifying a site of interaction between Survivin and HBXIP; and

determining whether a compound binds to said interaction site, thereby determining whether said compound is an agent that potentially alters the association of Survivin with HBXIP.

27. **(Withdrawn)** The method of Claim 26, further comprising confirming that said compound alters the association of Survivin with HBXIP by detecting an altered association between Survivin and HBXIP in the presence said compound.

28. **(Withdrawn)** The method of Claim 26, wherein said interaction site is a portion of Survivin that binds HBXIP.

29. **(Withdrawn)** The method of Claim 26, wherein said interaction site is a portion of HBXIP that binds Survivin.

30. **(Withdrawn)** The method of Claim 26, wherein said interaction site is identified using transverse relaxation-optimized spectroscopy.

31. **(Withdrawn)** The method of Claim 26, wherein said interaction site is identified using cross relaxation-enhanced polarization transfer.

32. **(Withdrawn)** The method of Claim 26, wherein nuclear magnetic resonance spectroscopy (NMR) is used to determine whether said compound binds to said interaction site.

33. **(Withdrawn)** The method of Claim 26, wherein fluorescence polarization assay (FPA) is used to determine whether said compound binds to said interaction site.

34. **(Withdrawn)** The method of Claim 26, wherein computational-docking studies are used to determine whether said compound binds to said interaction site.